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EXAMINER	
SHOMER, ISAAC	
ART UNIT	**PAPER NUMBER**
4121	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,494	COOK, GARY P.	
	Examiner	Art Unit	
	ISAAC SHOMER	4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18,20-33 and 35-50* is/are pending in the application.

4a) Of the above claim(s) *18,20-33 and 35-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7 April 2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a national stage entry of PCT/US04/22816 filed on 15 July 2004.

Priority

PCT/US04/22816 claims priority of provisional application 60/487,663, filed 15 July 2003 under 35 U.S.C. 119(e). Priority is granted from the filing date of the provisional application. Hence, the effective filing date of this application is 15 July 2003.

Information Disclosure Statement

The Information Disclosure Statement filed on 7 April 2009 has been considered by the examiner.

The Information Disclosure Appendix A, filed in 7 April 2009, has been considered by the examiner, but has been lined-through, because said appendix does not constitute a proper IDS. Furthermore, the documents mentioned in the body of the transmittal letter, filed on 7 April 2009 with the IDS, have been considered, but have been lined through, as said submissions do not constitute a proper IDS.

Election/Restriction

Applicant's election with traverse of Group I, claims 1-16, in the reply filed on 9 February 2009 is acknowledged. The traversal is on the ground(s) that there is no search burden. Furthermore, the traversal quotes MPEP 803. This is not found

persuasive because MPEP 803 does not apply to applications filed under 35 U.S.C. 371, as is the case in the instant application. MPEP 801 provides:

This chapter is limited to a discussion of the subject of restriction and double patenting under Title 35 of the United States Code and Title 37 of the Code of Federal regulations as it relates to national applications filed under 35 U.S.C. 111(a). The discussion of unity of invention under the Patent Cooperation Treaty Articles and Rules as it is applied as an International Searching Authority, International Preliminary Examining Authority, and in applications entering the National Stage under 35 U.S.C. 371 as a Designated or Elected Office in the U.S. Patent and Trademark Office is covered in Chapter 1800.

Furthermore, applicant has cancelled claims 17, 19, 34, and 51. Hence, the lack of unity requirement in light of Ignatious (US Patent 6,270,700) in view of Lewis et al. (US Patent 6,706,289) is withdrawn. However, there remains to be lack of unity for the following reasons:

The inventions listed as Groups I, III, and V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Group I is a method of making a comprising a bioactive agent, polymer, and organic salt, wherein the organic salt comprises an organic ion, as of page 11, last paragraph, of the response of applicant on 9 February 2009. The method of making said composition of claim 1 does not present a contribution over the prior art. As disclosed in Okada et al. (US Patent 5,814,342) the composition as disclosed of instant claim 1 is not novel (e.g., see 102 rejection below). As such, Group I does not share a special technical feature with the instant claims of Group III and V. Therefore, the claims are not so linked within the meaning of PCT Rule

13.2 so as to form a single inventive concept, and unity between Groups I, III, and V is broken.

Applicant further argued that the special technical feature is a process that utilizes an organic ion. Applicant further asserted that a special technical feature initially asserted by examiner, being a composition comprising a bioactive agent, polymer, and organic salt, is incorrect. The examiner points out that salts are compounds that comprise both cations and anions. In a case wherein either the cation or the anion of a salt is organic (wherein the term "organic" is well known in the art), said salt is organic. Therefore, the terms “organic ion” and “organic salt” comprise the same scope, as every organic ion is part of an organic salt.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 18, 20-33, and 35-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9 February 2009.

- Applicant's election with traverse of the following species
- Benzyl Alcohol, as of the cosolvent.
- Poly(vinyl alcohol) as the emulsifying agent.
- Ethyl acetate as the solvent.
- Microparticles as the controlled release composition.
- Poly(lactide-co-glycolide) as the polymer.
- Proteins as the bioactive agent.

- Oxytocin as the specific protein.
- Carboxylate as the organic ion.

in the reply filed on 9 February 2009 is acknowledged. The traversal is on the ground(s) that was used with respect to the groups. This is not found persuasive because: see supra response to the traversal.

The requirement is still deemed proper and is therefore made **FINAL**.

Rejections Under 35 U.S.C. 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "about" in claims 6 and 8 is a relative term which renders the claim indefinite. The term "about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicant must distinctly claim all numerical ranges.

According to MPEP 2173.05(b), the following is the case regarding the definiteness or lack thereof of the relative term "about."

A. “About”
In determining the range encompassed by the term "about", one must consider the context of the term as it is used in the specification and claims of the application. Ortho-

McNeil Pharm., Inc. v. Caraco Pharm. Labs., Ltd., 476 F.3d 1321, 1326, 81 USPQ2d 1427, 1432 (Fed. Cir. 2007). In< W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), the court held that a limitation defining the stretch rate of a plastic as “exceeding about 10% per second” is definite because infringement could clearly be assessed through the use of a stopwatch. However, the court held that claims reciting “at least about” were invalid for indefiniteness where there was close prior art and there was nothing in the specification, prosecution history, or the prior art to provide any indication as to what range of specific activity is covered by the term “about.” Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991).

According to the above paragraph, the court ruled that claims reciting "at least about" were indefinite when there was nothing in the specification, prosecution history, or prior art that indicates the specific range claimed. In the instant case, applicant has not specifically defined said range in the specification. In the instant case, the prior art, specifically Beaurline et al. (US Patent 5,112,604) teaches “a suitable preservative, e.g. 0.1% sodium benzoate.” As the prior art is close and applicant does not define the term "about" in the specification, instant claims 6 and 8 are indefinite pursuant to MPEP 2173.05(b), and applicant must define all claimed ranges.

Rejections Under 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-5, 7, and 9-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Okada et al. (US Patent 5,814,342) as evidenced by Franssen et al.

(Document U on the PTO-892). Whenever you make a 102 rejection using a "second" reference make sure you use the buzz words "as evidenced by" in the preamble.

According to MPEP 2131.01, multiple references may be used in a rejection under 35 U.S.C. 102 in the following cases:

2131.01 Multiple Reference 35 U.S.C. 102 Rejections
Normally, only one reference should be used in making a rejection under 35 U.S.C. 102. However, a 35 U.S.C. 102 rejection over multiple references has been held to be proper when the extra references are cited to:
(A) Prove the primary reference contains an "enabled disclosure; "
(B) Explain the meaning of a term used in the primary reference; or
(C) Show that a characteristic not disclosed in the reference is inherent.

The examiner asserts that the secondary reference, Franssen et al. (Document U on the PTO-892), will be used for reason (B), to explain the meaning of a term in the primary reference.

For ***claim 1***, Okada et al. (US Patent 5,814,342) (hereafter referred to as Okada) teaches, in Okada claim 5, a process for preparing a microcapsule exhibiting zero order release of a LH-RH analog, wherein said LH-RH analog is the bioactive agent. The method of making a microcapsule of Okada comprises an aqueous and an oil phase (organic phase), wherein said oil phase comprises a polymer. When Okada claim 5 is read in light of Okada column 4 lines 62-66, it is evident that the aqueous phase of claim 5 may further comprise an organic ion for the purpose of maintaining the stability (i.e. reducing the degradation) of the physiologically active peptide. All of these items read on the limitations of instant claim 1. The term "zero-order release" of claim 5 of Okada reads on the term "controlled release" of instant claim 1 because zero-order release is a form of release at a constant, controlled rate.

Instant claim 1 recites the limitation of “recovering said composition.” The examiner asserts that Okada did indeed recover said composition, as said composition was taught in claim 1 of Okada. If Okada had been unable to recover the composition made in claim 5, then Okada would have been unable to claim said composition.

For ***claims 4 and 5***, Okada, in claim 7, teaches a method of making a microcapsule as to claim 5 of Okada, further comprising an emulsifying agent, wherein said emulsifying agent is polyvinyl alcohol.

For ***claim 7***, Okada, in claim 5, teaches an oil phase. When read in light of column 4 lines 1-10, it is evident that said oil phase comprises an organic solvent to dissolve the polymer of the organic phase. Column 4 line 8 teaches that said solvent may be ethyl acetate.

For ***claim 9 and 10***, Okada, in claim 5, teaches a method of preparing a microcapsule. The examiner asserts that the term "microcapsule" as used by Okada reads on the term "microparticle" as of instant claim 9, in light of Franssen et al. (Document U on the PTO-892), in the abstract, which uses the term "microparticle" and "microcapsule" synonymously." When claim 5 of Okada is read in light of column 1 line 37, it is evident that said microcapsules are biodegradable.

For ***claim 11***, Okada, claim 5, teaches an organic phase comprising a polymer wherein said polymer may be a “copolymer of lactic acid and glycolic acid.” This reads on the elected species, poly(lactide-co-glycolide)s.

For ***claims 12 and 13***, Okada claim 5 teaches a microcapsule which releases a luteinizing hormone-releasing analog as the bioactive agent. When read in light of

column 2 line 39, it is evident that said bioactive agent may be oxytocin, which reads on the elected species of instant claims 12 and 13.

For ***claims 14 and 15***, Okada claim 5, when read in light of column 8 lines 1-2 teaches combining the organic and aqueous phases to yield a water-oil-water (W/O/W) emulsion.

For ***claim 16***, Claim 5 of Okada teaches a process for preparing a microcapsule. When claim 5 is read in light of Okada column 4 lines 62-66, it is evident that the aqueous phase of claim 5 may further comprise an organic ion for the purpose of maintaining the stability (i.e. reducing the degradation) of the physiologically active peptide. Examples given of organic acids or ions thereof comprise acetic acid, oxalic acid, and citric acid. All of these read on the species “carboxylate” in instant claim 16. It should further be pointed out that, although the instant application teaches an "organic ion" as if the ion is deprotonated, the instant specification, on the table on page 21 entitled "Formulation D2," teaches a solution of sodium acetate at pH 4. The examiner asserts that the pKa of acetic acid is greater than 4, causing most molecules of acetic acid to be protonated at said pH. Hence, the examiner asserts that the term “organic ion” refers to both an organic anion and its conjugate acid. In light of this assertion, the elements of claim 5 of Okada in light of Okada column 4 lines 62-66.

Rejections Under 35 U.S.C. 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-3 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Okada in view of Lyons et al. (US 6,194,006 B1).

See supra rejection of claim 1, 4, 5, 7, 9-16. Okada also refers to the presence of benzyl alcohol in the controlled release formulation, in column 5 line 6 of the disclosure of Okada. However, Okada utilizes benzyl alcohol as a preservative, and not as a cosolvent.

For ***claim 2***, Okada fails to teach the presence of a cosolvent in the organic phase.

For ***claim 3***, Okada also fails to teach benzyl alcohol as the cosolvent of claim 2.

For ***claim 6***, Okada fails to teach a method of instant claim 4 wherein said emulsifying agent is at a final concentration of 0.1% to 10% w/w.

However Lyons et al. teach the limitations that are deficient in Okada.

For ***claims 2 and 3***, Lyons et al. (US 6,194,006 B1) (hereafter referred to as Lyons) teaches, in claim 43, a controlled release formulation comprising a solvent mixture of ethyl acetate and benzyl alcohol. This reads on the additional limitations of instant claims 2 and 3 in light of the species selection of benzyl alcohol reading upon claim 3.

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the instant invention was made to have combined the inventions of Okada and Lyons. This is because according to Lyons, column 2 lines 40-47, the microparticles

prepared by the method of Lyons have a selected release profile wherein there is a controlled release profile of an active agent contained in microparticles. According to column 5, lines 44-49, the presence of benzyl alcohol as a solvent reduces the glass transition temperature, or T_g of the microparticles. The use of benzyl alcohol to reduce the apparent glass transition temperature of the microparticles makes it possible to wash said microparticles without having them agglomerate. Lyons, column 11 lines 44-50 shows that the use of an extraction method wherein the glass transition temperature of the solvent starts out as being higher than that of the microparticle, which is shown by Lyons to reduce agglomeration. The examiner asserts that increased dispersion and reduced agglomeration beneficially affects the release profile of the drug, as of column 5 lines 27-29 of Lyons. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the methods used by Lyons into the microparticles of Okada. Furthermore, in light of Lyons, one of ordinary skill in the art would have had a reasonable expectation of success in increasing dispersion and decreasing agglomeration with regards to the addition of benzyl alcohol as a cosolvent (as of Lyons), to the microparticles of Okada.

Further, with regard to ***claim 6***, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to alter the w/w % disclosed by Okada to achieve the currently claimed w/w/% because such a manipulation represents mere routine optimization. See MPEP 2144.05:

> A. Optimization Within Prior Art Conditions or Through Routine Experimentation Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." … For

more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Here, no indication of "criticality" has been set forth that would otherwise indicate that such optimization would be anything other than routine. Furthermore, the methods of filtration and drying are similar between the prior and instant examples.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Okada in view of Beaurline et al. (US Patent 5,112,604) as evidenced by Johnson (Materials Safety Data Sheet, Document V on the PTO-892).

See supra rejection of claim 1, 4, 5, 7, 9-16 under 35 U.S.C. 102. Furthermore, Okada discloses a formulation of claim 1 where the organic ion is a preservative, which reads on reducing degradation of the active agent as of instant claim 1.

For ***claim 8***, Okada fails to disclose an example where said organic ion is present in the amount of 0.1 to 1000 mM, as of instant claim 8.

However Beaurline et al.. teach the limitations that are deficient in Okada.

For ***claim 8***, Beaurline et al. (US Patent 5,112,604) (hereafter referred to as Bearuline) teaches a suspension used for controlled release of a drug (see claim 8 of Beaurline), wherein said suspension comprises 0.1% by weight of sodium benzoate dissolved in a 70% sorbitol in water solution. Sodium benzoate reads on the organic ion of instant claims 1 and 8. The concentration 0.1% by weight is equivalent to 6.9 mmol/L provided that the density of the suspension is 1 g/mL (equivalent to that of water). As evidenced by Johnson (Materials Safety Data Sheet, Document V on the PTO-892), the

density of aqueous 70% sorbitol is 1.29 g/mL. Hence, the molarity of sodium benzoate in said solution is (0.1 g benzoate / 100 g solution)*(1 mol/144 g)*(1 mL solution/1.29 g solution) = 9.0 mmol/L or 9.0 mM, reading on the concentration range of instant claim 8.

It would have been prima facie obvious for one of ordinary skill at the time the invention was made to have combined the inventions of Okada and Beaurline. According to Beaurline, column 2 lines 58-66, the value of 0.1% sodium benzoate to be used as a preservative is found in commercially available Simple Syrup NF. Hence, one of ordinary skill in the art should have been aware that sodium benzoate in this concentration is well known in the art for the purpose of a preservative. Given that Okada, column 5 line 4 teaches that a preservative may be used, one of ordinary skill in the art would have a reason to combine this with Bearuline, which specifies in greater detail as to a preservative that may be used along with its concentration. Hence, it would have been prima facie obvious for one of ordinary skill in the art to have combined the inventions of Okada and Beaurline at the time the invention was made. Furthermore, one of ordinary skill in the art would have had a reasonable expectation of success regarding the addition of sodium benzoate for use as a preservative, as of Bearuline, to the composition of Okada.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ISAAC SHOMER whose telephone number is (571)270-

7671. The examiner can normally be reached on Monday - Thursday 7:30AM - 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571)272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/I. S./
Examiner, Art Unit 4121

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4121